

Bispectral Index Monitoring of Sedation Depth in Pediatric Dental Patients

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The bispectral index (BIS) monitor records electroencephalogram waveforms and provides an objective measure of the hypnotic effect of a sedative drug on brain activity. The aim of this pilot study was to use the BIS monitor to evaluate the depth of procedural sedation in pediatric dental patients and to assess if the BIS monitor readings correlate with a validated pediatric sedation scale, the University of Michigan Sedation Scale (UMSS), in determining the level of sedation in these patients. Thirty-five pediatric dental patients requiring sedation were studied prospectively. A baseline BIS reading was obtained and during the procedure an independent observer recorded the BIS every 5 minutes. The operator, who was blinded to the BIS results, determined the UMSS scale at the same 5-minute interval. The patients were monitored postoperatively for 1 hour. There was a significant but moderate correlation between BIS values and UMSS scores (Spearman's rank correlation $r = -0.574$, $P < .0001$). Percentage of agreement and kappa coefficient using all the observations were also calculated. The percentage of agreement was 37.8%, the kappa coefficient was 0.18 ($P < .0001$), and the weighted kappa coefficient 0.26 ($P < .0001$). A lack of correlation was noted between the deeper levels of UMSS sedation scores and BIS values. This study demonstrated a significant correlation between BIS values and the UMSS score in pediatric dental patients undergoing mild to moderate sedation. Based on our results, it appears that the BIS monitor may be useful during mild or moderate sedations to establish the level of sedation objectively without the need to stimulate the patient.

Key Words: Bispectral index monitor; Pediatric sedation; University of Michigan Sedation Scale; Pediatric dentistry.

The use of pharmac-sedation is an important adjunct in the behavior management of pediatric dental patients. During the last decade there has been an increase in dental procedures performed with sedation in outpatient dental offices^{1–6}; therefore, the American Academy of Pediatrics and the American Academy of Pediatric Dentistry (AAPD) have published a series of guidelines for the monitoring and management of pediatric patients during and after sedations.^{7,8} According to these guidelines, a clinician must be able to rescue the patient from a deeper level of sedation than that intended for a procedure and therefore must be able to recognize the level of seda-

tion of the patient. Additionally, the guidelines require clinicians to record the depth of sedation for their patients during the sedation procedure.⁷

Accurate assessment of the depth of sedation requires a tool that is reliable and valid, but also easy to use in a clinical setting. A variety of sedation scoring systems have been developed to measure the depth of sedation for both research and clinical settings. The more commonly used scales include the University of Michigan Sedation Scale (UMSS),^{9,10} the Observer's Assessment of Alertness/Sedation (OAA/S),¹¹ the Ramsay Sedation Score,¹² and the Houpt Scale.¹³ These sedation scales have limitations in clinical practice because of observer variance in the subjective assessment and the disruptive effect of stimuli that need to be given to assess the depth of sedation. The UMSS is a simple 5-point observational scale that assesses

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Table 1. University of Michigan Sedation Scale (UMSS) Scoring

UMSS Score	Description
0	Awake/alert
1	Minimally sedated: tired/sleepy, appropriate response to verbal conversation and or sound (calling child's name)
2	Moderately sedated: somnolent/sleeping, easily aroused with light tactile stimulation (lightly touching arm, face, or leg)
3	Deeply sedated: deep sleep arousable only with significant physical stimulation (tickling their feet)
4	Unarousable: unresponsive to foot tickle

the level of alertness on a 5-point scale, ranging from 0 (wide awake) to 4 (unarousable with deep stimulation) (Table 1). This scale was devised to provide a standardized method for assessing sedation over the entire continuum from awake to unarousable. It facilitates the rapid assessment and documentation of the depth of sedation in all patients who receive 1 or more sedative agents for diagnostic or therapeutic procedures. It scores the patient's response to stimuli in a manner consistent with the nationally recognized definitions of sedation. It has been tested for interrater and test-retest reliability and construct and criterion validity in small samples of children aged 6 months to 12 years, supporting its use during procedural sedation.^{10,14,15}

The use of the electroencephalogram (EEG) to monitor the level of sedation is a noninvasive tool that is based on the principal that EEG waveforms change with the level of alertness.¹⁶ In general, when a patient is awake the EEG waveforms are of high frequency and low amplitude, and when a patient is deeply sedated the frequency decreases and the amplitude increases. The bispectral index (BIS) monitor (Aspect Medical Systems, Newton, Mass) is an FDA-approved monitor that has been used in clinical practice since 1997.¹⁷ It gathers processed EEG parameters to provide a numeric measure of the hypnotic effect of anesthetic or sedative drugs on brain activity. It is derived from the EEG by a computer algorithm that produces a single numeric value, scaled from 0 to 100.¹⁸ According to the manufacturer, a BIS score of >90 indicates an awake patient; 71–90, mild to moderate sedation; 61–70, deep sedation; and 40–60, general anesthesia. The goal of the BIS monitor is to provide an objective, quantitative measurement of the level of hypnosis.¹⁶ The utility of the BIS monitor during general anesthesia has been validated in multiple pediatric studies.^{19–21} Recent studies have shown BIS scores to correlate with observational sedation scores during moderate and deep sedation in pediatric pa-

tients.^{15,22–25} McDermott et al¹⁵ performed a study on 86 children under 12 years of age who underwent moderate or deep sedation and compared the BIS scores to the UMSS. In 2005, Shields et al²² correlated the BIS scores with the UMSS in 38 children undergoing sedation for gastrointestinal procedures. Sadhasivam et al²⁴ correlated the BIS scores with the UMSS and OAA/S scores in 96 children aged 1–12 years undergoing diagnostic or interventional procedure. In a larger scale study of 248 children, Malviya et al²⁵ correlated the BIS scores with the UMSS and evaluated age and sedative agent differences.

In the dental literature, few studies have been published on the use of the BIS monitor during outpatient procedural sedations. Sandler and Sparks²⁶ analyzed BIS results and correlated them with OAA/S scale in 25 patients, aged between 18 and 65 years old, undergoing IV sedation for third molar extractions. Morse et al²⁷ compared BIS scores to the OAA/S scale in 22 patients, with a mean age of 40 years, while receiving IV sedation with midazolam or midazolam and ketamine for oral surgery procedures. In the pediatric dental literature specifically, fewer studies have been published. The first study, done by Religa et al²⁸ and using the AAPD guidelines, correlated BIS scores with level of sedation in 34 pediatric patients undergoing oral sedation with the combination of chloral hydrate, meperidine, and hydroxyzine for dental restorations. Overly et al²⁹ analyzed BIS scores for 16 patients undergoing deep sedation with IV medications for oral surgery and correlated them with the OAA/S scale. Recently, Messieha et al³⁰ studied the usefulness of the BIS monitor in reducing recovery and postanesthesia care unit discharge time for pediatric patients undergoing dental rehabilitation with general anesthesia after receiving IM ketamine or oral midazolam pre-sedation. To date, no studies correlating the UMSS with the BIS monitor readings in pediatric dental patients undergoing mild to moderate sedation have been published.

The purpose of this pilot study was to use the BIS monitor to evaluate the depth of sedation achieved during mild to moderate sedation (oral and transmucosal sedations) in pediatric dental patients undergoing dental restorations. Additionally, we wanted to assess if the BIS monitor reading correlated with the UMSS in determining the level of sedation in these patients.

MATERIALS AND METHODS

With approval from the Yale-New Haven Hospital Human Investigation Committee, parental written in-

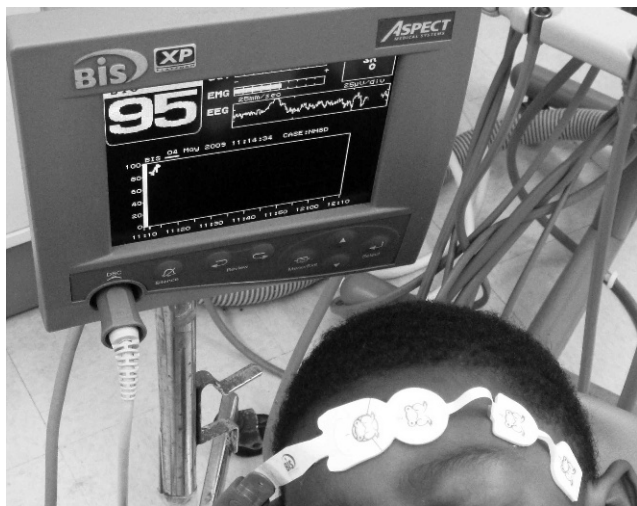


Figure 1. Clinical photograph of BIS monitor and 4 electrodes placed on patient's forehead.

formed consent was obtained for each of the 35 pediatric patients enrolled in this observational single-blinded study. The subjects were nonobese children between the ages of 2 and 7 years old, American Society of Anesthesiologists (ASA) I or II with a Mallampati score of I or II, and a Tonsil size I or II. They followed strict nil per os (NPO) guidelines, which include light meal >6 hours and clear liquids >2 hours, and had a current (<30 days old) history and physical exam. All patients were scheduled to undergo routine elective dental restorations under mild or moderate sedation at Yale-New Haven Pediatric Dentistry Center. Exclusion criteria included patients with severe developmental delay, known neurological disorders (such as hemiplegia, demyelinating disorders, stroke, and cerebral palsy), and marked skin sensitivity that could react to the adhesive in the electrodes. The operator (pediatric dentistry resident performing the procedure) selected and administered the sedation regimens based on the patient's weight, age, and treatment needs. The following sedation regimens were utilized:

- Regimen 1: chloral hydrate 50 mg/kg + meperidine 0.5 mg/kg + hydroxyzine 1 mg/kg (oral)
- Regimen 2: fentanyl 200 mcg (20–30-kg patients) or 400 mcg (>30-kg patients) (transmucosal) + hydroxyzine 1 mg/kg (oral)
- Regimen 3: hydroxyzine 3 mg/kg (oral)
- Regimen 4: midazolam 0.3–0.7 mg/kg + hydroxyzine 1 mg/kg (oral)

The BIS monitor (A-2000 BIS, Aspect) probe with the 4 external electrodes was applied to the patient's forehead (frontotemporal region) to obtain 1 baseline BIS reading before the administration of the sedation medications (Figure 1). After the appropriate latency

period (45 minutes to 1 hour), the patient was positioned in the protective stabilizer with a shoulder roll; the blood pressure cuff, pulse oximeter, and precordial stethoscope were placed; and the BIS probe was reattached to the monitor. All patients received nitrous oxide sedation via a nasal hood, with a concentration of 70% N₂O and 30% O₂ at a 3 L/min flow rate, for the duration of the procedure. An independent observer monitored and recorded the blood pressure, heart rate, respiratory rate, oxygen saturation, and BIS readings intraoperatively every 5 minutes. The operator, who was blinded to the BIS monitor, determined the UMSS scale at the same 5-minute interval. During the procedure, specific events such as local anesthetic injection, rubber dam clamp placement, and extractions were recorded. All restorative procedures were completed utilizing a rubber dam, and throat pack was always in place for extractions. After the procedure was completed, patients were monitored in the recovery room for 1 hour; the blood pressure, heart rate, respiratory rate, oxygen saturation, BIS, UMSS, and a modified Aldrete score were recorded every 15 minutes. Patients were discharged when their Aldrete scores were back to baseline.

The data analysis was performed using statistical software SAS 9.1 (SAS, Cary, NC). The relationships between all the BIS values and UMSS scores were first evaluated using Spearman's rho correlation coefficient because of skewed distribution of BIS. Then within-subject correlation coefficient was calculated after accounting for the dependency of repeated measures. Kappa and weighted kappa statistics were also calculated to assess agreement between BIS categorized based on clinical relevance and UMSS scores, which corrects for chance of agreement.

Additionally, repeated measures analysis was performed with BIS values as dependent variable, and age, gender, and regimen were adjusted in the model. Serial correlation structure was used to account for the within-subject correlation from multiple observations per patient, followed by post hoc pair-wise comparisons to determine differences in BIS values between each UMSS score group.

RESULTS

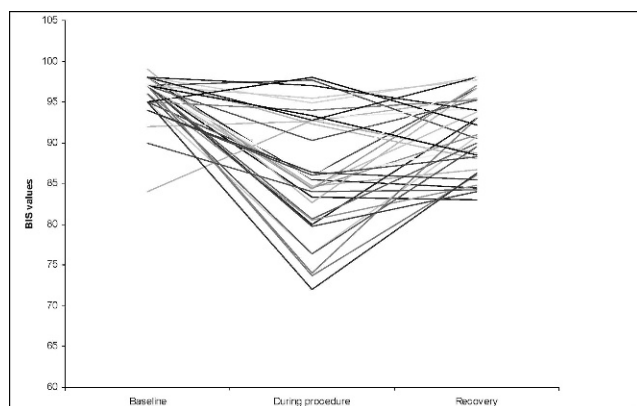
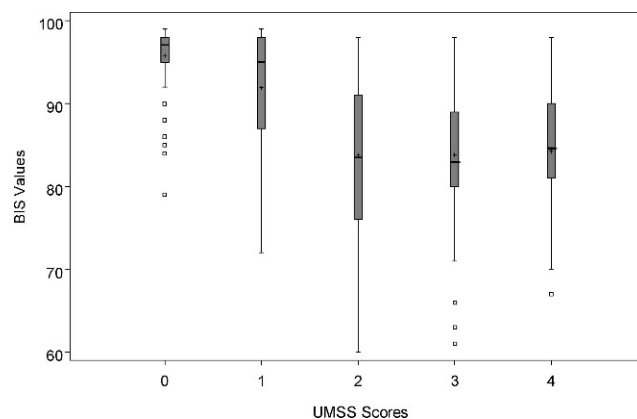
We enrolled 35 patients in the study prospectively, producing a total of 455 observations of the BIS and UMSS indexes. All enrolled patients completed the study. Table 2 summarizes the patient demographics and their clinical characteristics. Patients were studied for 2.5 ± 0.3 hours with range from 2 to 3.25 hours, and 13 ± 3 observations (UMSS and BIS score) were

Table 2. Patient Demographic and Clinical Characteristics*

Characteristics	All Patients (N = 35)
Age, y	4.2 ± 1.1
Gender	
Male	16 (45.7%)
Female	19 (54.3%)
Weight, kg	17.2 ± 3.4
Sedation regimen	
Chloral hydrate/meperidine/hydroxyzine	24 (68.6%)
Fentanyl/hydroxyzine	9 (25.7%)
Hydroxyzine	1 (2.9%)
Midazolam/hydroxyzine	1 (2.9%)

* Continuous variables are presented as mean ± SD; categorical variables are presented as frequency (%).

recorded for each patient, with a range from 8 to 21. Distinct stages during the procedure were noted; these included start of procedure, local anesthetic injection, rubber dam clamp placement, tooth extraction (if applicable), and recovery. The number of observations (UMSS and BIS score) was very unbalanced across different stages of the study. Of the total 455 observations, 35 (7.7%) were at baseline, 176 (38.7%) were at start of procedure, 51 (11.2%) were at local anesthetic injection, 52 (11.4%) were at rubber dam clamp placement, 1 (0.2%) was at tooth extraction and 140 (30.8%) were during recovery. The BIS values ranged from 60 to 99 with a mean value of 88 ± 8.9 . For the UMSS the values were distributed as follows: UMSS score 0, 112 (24.6%); UMSS score 1, 95 (20.9%); UMSS score 2, 142 (31.2%); UMSS score 3, 88 (19.3%); and UMSS score 4, 18 (4.0%). The construct validity of the BIS values was demonstrated by the appropriate changes in BIS value during baseline (before sedation administration) and the start of dental procedure, and also at recovery period (Figure 2). A significant decline in BIS

**Figure 2.** Results of BIS values at the different stages of the procedure (baseline, start of procedure, and recovery) for all patients ($n = 35$).**Figure 3.** Box and whisker plot of bispectral index values for each University of Michigan Sedation Scale Score.

value from baseline to start of procedure was found ($P < .0001$), and the BIS values increased from during procedure to recovery ($P < .0001$). No significant difference was shown between BIS values at baseline and recovery ($P = .52$).

The relationship between all the BIS values and all the UMSS scores in the study is shown in Figure 3. There was a significant but moderate correlation between BIS values and UMSS scores (Spearman's rank correlation $r = -0.574$, $P < .0001$). Overall the BIS values tended to decrease with increasing values of UMSS score. The within-subject correlation coefficient was calculated (correlation coefficient $r = -0.528$ with $P < .0001$), which means that within an individual an increase in BIS value was associated with a decrease in UMSS score.

After controlling for age, gender, and regimen administered (combining regimens 2, 3, and 4), a significant difference in BIS values was found between UMSS 0 and 1, 0 and 2, 0 and 3, 0 and 4, 1 and 2, 1 and 3, and 1 and 4, but not between UMSS 2 and 3, 2 and 4, or 3 and 4 (Figure 4). Similar results were obtained after UMSS scores 3 and 4 were combined. The percentage of agreement and kappa coefficient were also calculated. The clinically relevant manufacturer-suggested BIS categories were used and the UMSS score 3 and 4 were combined in order to calculate the percentage of agreement and kappa coefficient. Percentage of agreement was 37.8%, kappa coefficient 0.18 ($P < .0001$) with 95% confidence interval 0.13–0.23, and weighted kappa coefficient 0.26 ($P < .0001$) with 95% confidence interval 0.21–0.30 (Table 3).

DISCUSSION

The results of this study demonstrate that the BIS may be a valid monitor of the depth of sedation for children undergoing dental restorations with mild to moderate

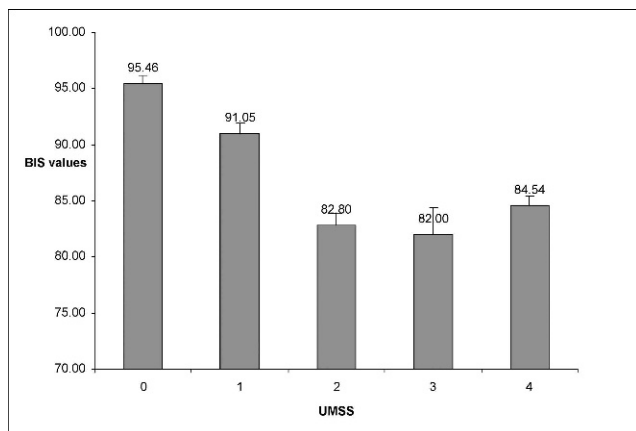


Figure 4. Estimated bispectral index values and mean standard error for each University of Michigan Sedation Scale Score (UMSS) after adjusting for age, regimen (combined regimen 2, 3, and 4) and gender. Significant differences in BIS values were demonstrated between UMSS 0 and 1 (difference 4.4 with 95% CI 2.3–6.5, $P < .0001$), and 1 and 2 (difference 6.5 with 95% CI 4.4–8.6, $P < .0001$), but not between UMSS 2 and 3 (difference 1.7 with 95% CI –0.6 to 4.1, $P = .15$) and UMSS 3 and 4 (difference 0.8 with 95% CI –4 to 5.6, $P = .75$).

sedation. The BIS values correlated significantly with the UMSS scores. The BIS has several potential advantages over observational clinical sedation scoring systems: it is objective, quantitative, easy to use, and free of observer bias, and does not require the use of stimuli that can result in patient responses that disrupt the procedure for which the child is sedated. These results are consistent with previous studies that validated the BIS against UMSS in sedated children.^{15,24} There has been only 1 other study utilizing the BIS for oral sedation of pediatric dental patients. Religa et al²⁸ found an association between BIS values and behavior during oral sedations, using the AAPD sedation guidelines, which are a scale based on behavioral responsiveness to stimuli. Our study differs from this one in that we compared BIS values to a validated pediatric sedation scale, the UMSS. Also, in their study no baseline values for BIS were obtained, there was no blinding to the BIS data, and they did not correlate both in-

struments (BIS and AAPD sedation scale); they only associated the observed behaviors to the level of sedation according to the BIS value and AAPD sedation scale. Two other studies have analyzed BIS values to sedation scales in pediatric and adult patients undergoing oral surgery procedures. Overly et al²⁹ compared BIS values to the OAA/S¹¹ and Ramsey¹² scales, both validated scales in pediatric dental patients undergoing oral surgery. Their sample was smaller (16 patients) but they had blinding and were able to obtain a repeated-measures regression analysis and found a positive correlation. Sandler and Sparks²⁶ compared BIS values to OAA/S scores in 25 adult patients undergoing IV sedation for third molar extractions. They also found a positive correlation.

A problem in validating the BIS monitor as an assessment of sedation depth is the absence of a gold standard for comparison. A variety of clinical scoring systems exist and have been utilized in adults, but few have been validated in children. The UMSS has successfully been validated for measuring sedation depth in children.¹⁰ However, these scales are subject to interobserver variability, especially in the middle of the scale. This can explain the lack of significant difference with the repeated-measure analysis between the BIS values and UMSS 2 and 3, 2 and 4, and 3 and 4. In our study we also had 7 operators assigning the UMSS scores, which could have increased the variability. Interestingly, Malviya et al⁹ also compared the BIS to UMSS in pediatric patients and found a lack of correlation between the BIS and UMSS scores of 2 and 3. Comparisons between BIS and other observational tools have shown similar variability in the midranges of sedation.^{31,32} In our study there was also lack of correlation between the deeper levels of UMSS sedation scores and BIS values. This phenomenon can be explained by the relatively rare occurrence of the deeper levels of sedation (only 88 [19.3%] for UMSS 3 and 18 [4.0%] for UMSS 4 reported, which occurred to 16 patients and 3 patients respectively) with the use of sedative agents and doses that usually cause only mild to moderate sedation. Interestingly, there were

Table 3. The Agreement Between UMSS and BIS Values With the UMSS 3 and 4 Combined

BIS	UMSS Score			
	0 = Awake/ Alert	1 = Minimally Sedated	2 = Moderately Sedated	3 = Deeply Sedated/ 4 = Unarousable
Awake/alert (91–100)	105 (23.08%)	65 (14.29%)	42 (9.23%)	27 (5.93%)
Minimally sedated (81–90)	6 (1.32%)	24 (5.27%)	56 (12.31%)	55 (12.09%)
Moderately sedated (71–80)	1 (0.22%)	6 (1.32%)	39 (8.57%)	20 (4.40%)
Deeply sedated/unarousable (70 and below)	0 (0.00%)	0 (0.00%)	5 (1.10%)	4 (0.88%)

* UMSS indicates University of Michigan Sedation Scale; BIS, bispectral index.

27 “deeply sedated” or “unarousable” observations where the BIS readings were in the “awake-alert” category.

Some clinical scoring systems have the disadvantage of requiring the application of additional verbal or noxious stimuli to assess the level of sedation during the procedure. Clinicians are reluctant to apply vigorous physical stimuli to children undergoing mild to moderate sedation for fear of the accompanying patient response of undesirable movements. However, the UMSS requires the repeated application of a uniform, quantifiable stimulus of the same intensity (light touch to face and arm). Standardizing the stimulus among the 7 operators is difficult and may have resulted in underestimating or overestimating the level of sedation. This also may have contributed to the lack of agreement between some of the sedation scales and the BIS values.

We were able to establish the validity of the BIS monitor by determining the construct validity of this instrument. The validity of the BIS value as a measure of sedation was supported by the decrease in BIS values after the administration of the sedative agent and the subsequent increase as the patient returned to baseline and was discharged.

Limitations of this study included the sample size, unequal distribution of patients for each different sedation regimen, variety of dental procedures performed, and different lengths of procedures, all of which could confound the results. For example, although we attempted to control for sedation regimen in our analysis because of the limited number of patients on 3 of the sedation regimens utilized, we had to combine the results for these in order to control for drug effect. This resulted in no difference in BIS values between the most commonly used regimen (chloral hydrate/meperidine/hydroxyzine) and the other 3 regimens. Further studies would be indicated to define the relationship between BIS values and each sedation regimen in a larger sample of patients. Additionally, the sedation regimens utilized were intended only for mild to moderate sedation; no conclusions could be obtained about the value of the BIS for deeper sedations. The use of the BIS monitor in deeper sedation could be established by studying the correlation of BIS values in pediatric dental patients undergoing IV sedation.

Known limitations of the BIS monitor include signal quality and electrical interference.¹⁷ A low signal-to-noise ratio is indicative of poor quality input into the monitor, and this can alter the readings. Additionally, the accuracy of the BIS scores can be affected by the electromyographic activity. A high electromyographic activity can be present in sedated patients, interfering with EEG signal acquisition and falsely elevating the

BIS values. It is unknown what type of effect electromyographic activity, particularly on the temporalis muscle, has on the BIS values during dental or oral surgery procedures. Technically the BIS monitor can be somewhat difficult to use in children because some are uncomfortable with the amount of pressure needed to apply the monitor correctly. Religa et al²⁸ in their study lost 33% of the data because of the difficulty in applying and getting usable information from the BIS monitor. We did not encounter as many problems with the use of the monitor in our patient population and were able to obtain data on all 35 enrolled subjects. Another shortcoming of the BIS monitor is that it has been observed to lag approximately 60 seconds behind the clinical situation,^{33,34} so that the reading reflects the level of consciousness about 60 seconds in the past.

Ongoing assessment of the depth of sedation is very important for early identification of the patient's progression into deep sedation and the potential loss of protective reflexes. The AAPD, American Academy of Pediatrics, and ASA guidelines require ongoing assessment of the depth of sedation throughout the procedure. The BIS monitor may provide an additional objective measure of sedation depth to ensure patient safety.

CONCLUSIONS

This study demonstrated the significant correlation between BIS values and the UMSS score in pediatric dental patients undergoing mild to moderate sedation. It appears that the BIS monitor may be useful in pediatric dentistry during mild or moderate sedations to establish the level of sedation objectively without the need to stimulate the patient.

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